Office Action Summary	Application No.	Applicant(s)	
	10/731,224	DESAI ET AL.	
	Examiner	Art Unit	
	Marsha M. Tsay	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-18,84 and 97-225* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *See Continuation Sheet* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *02/23/07; 06/13/07; 12/20/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 4,15-18,102,108-127,143-147,149-151,154-181,184-188,191-195,198-202,205,208,212-216,220,221 and 224.

Continuation of Disposition of Claims: Claims rejected are 1,5-14,84,97-101,103-107,128-142,148,152,153,182,183,189,190,196,197,203,204,206,207,209-211,217-219,222,223 and 225.

Applicant's election without traverse of Group I, claims 1, 4-17, 84, 97-107, 128-148, 152-160, 182-215, 217-219, 222-223, 225, to taxane and the (sub)species paclitaxel, in the reply filed on December 20, 2007 is acknowledged.

Claims 4, 15-18, 102, 108-127, 143-147, 149-151, 154-181, 184-188, 191-195, 198-202, 205, 208, 212-216, 220-221, 224 are withdrawn. Claims 1, 5-14, 84, 97-101, 103-107, 128-142, 148, 152-153, 182-183, 189-190, 196-197, 203-204, 206-207, 209-211, 217-219, 222-223, 225 read on the elected (sub)species, and are currently under examination.

Priority: The priority date is December 9, 2002.

Objections and Rejections

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 84, 103, 105, 107, and their dependent claims are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an effective amount of human serum albumin to reduce one or more side effects of a pharmaceutical agent in a human, does not reasonably provide enablement for an effective amount of albumin from any source and/or species to reduce one or more side effects of a pharmaceutical agent in a human. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The scope of the instant claims is not commensurate with the enablement of the instant disclosure, because practice of the claimed invention would require undue experimentation by an artisan of ordinary skill in the art to ascertain which other albumin proteins, besides human serum albumin, and their effective amounts would reduce one or side effects of a pharmaceutical agent in a human. Thus, it could include albumin from any species. Thus for the instant claimed invention, it would require an undue burden of experimentation for a skilled artisan to determine exactly which type of albumin protein and the amount that is effective to reduce one or more side effects of a pharmaceutical agent in a human.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

In the instant case the quantity of experimentation would be large since there are myriad albumin proteins to choose from. The amount of guidance in the specification is zero with regard to which albumin protein, besides human serum albumin, and an amount that is effective to reduce one or more side effects of a pharmaceutical agent in a human. The working examples appear to only disclose the use of an effective amount of human serum albumin. The nature of the invention is such that the same protein from a different species may or may not have the same effect when administered to a human. The state of the prior art is that proteins from different species may or may not have an amount that is effective to reduce one or more side effects of a pharmaceutical agent in a human. The relative level of skill in this art is very high. The predictability as to the effective amount of an albumin from any species to reduce one or more side effects of a pharmaceutical agent in a human is zero.

When the factors are considered in their entirety, the Wands analysis dictates a finding of undue experimentation and thus, the claim is not enabled.

Claims 1, 84, 103, 105, 107, and their dependent claims are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The claims are drawn to compositions comprising a pharmaceutical agent, albumin in an amount effective to reduce one or more side effects, and deferoxamine in an amount effective to inhibit microbial growth. *Vas-Cath Inc. V. Mahurkar*, 19USPQ2d 1111, clearly states that

"applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed."* The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." As stated above, albumin in an amount effective to reduce one or more side effects of administering a pharmaceutical agent into humans. However, the skilled artisan cannot necessarily envision all different sources of albumin protein and their amounts that are effective to reduce one or more side effects because nowhere in the specification is it described which other sources of albumin, besides human serum albumin, and their effective amounts, are effective to reduce one or more side effects of a pharmaceutical agent in a human, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the methods of making the claimed invention. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating or making it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 5-14, 84, 97-101, 103-107, 128-142, 148, 152-153, 182-183, 189-190, 196-197, 203-204, 206-207, 209-211, 217-219, 222-223, 225 are rejected under 35 U.S.C. 112, second

paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 84, 103, 105, 107, and their dependent claims are drawn to a pharmaceutical composition comprising a pharmaceutical agent and a pharmaceutical acceptable carrier. However, as currently written, the claims appear to regard both albumin and deferoxamine as pharmaceutical carriers. Therefore, either the composition must comprise more than one carrier or one of the constituents should be deleted. Further clarification is requested.

Claims 1 and 134 recite improper Markush language. The term "and" should be inserted before "mycophenolic acids."

Claims 84, 128-129, 137-138 recite a ratio of albumin to a pharmaceutical agent is about 18:1, 15:1, or 9:1 or less, respectively. The claims are indefinite because there is no lower limit to the ratio range, therefore, the "or less" limitation can comprise a weight ratio of 0 to 0, thereby rendering the claims indefinite since the instant claims are drawn to a composition comprising an effective amount of albumin and a pharmaceutical agent.

Claims 148, 152-153 recite the nanoparticles have a mean size of less than about 200 nm. The claim are indefinite because there is no lower limit to the nanoparticle's mean size, therefore, the nanoparticle mean size can be 0 nm, which would not make any sense. Further, it is unclear what is meant by "mean size", i.e. if mean size refers to diameter.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 84, 128-129, 132-133 are rejected under 35 U.S.C. 102(b) as being anticipated by Yang et al. (1993 Biochemical Pharmacology 46(2): 336-339; previously cited). Claim 84, line 6, recites the weight ratio of albumin to pharmaceutical agent is about 18:1 or less. Therefore, the instant claim can encompass a weight ratio of 0. Yang et al. teach a composition comprising human serum albumin, dihydroartemisinin, and deferoxamine (DFO, 1 mM) (p. 336 col. 2; claims 84, 128, 129, 132-133). Yang et al. do not specifically teach the role or function of deferoxamine in the composition. However, the properties of inhibiting microbial growth (claim 84) are properties that are inherent to deferoxamine. It is known in the art that artemisinin is an effective anti-cancer agent (Singh et al. 2001 Life Sciences 70: 49-56; previously cited).

Claims 84, 128-129, 132 are rejected under 35 U.S.C. 102(b) as being anticipated by Ritov et al. (2001 Diabetes 50: 1253-1262; previously cited). Claim 84, line 6, recites the weight ratio of albumin to pharmaceutical agent is about 18:1 or less. Therefore, the instant claim can encompass a weight ratio of 0. Ritov et al. teach a composition comprising 100 mmol/l mannitol, 5.0 mg/ml bovine serum albumin (BSA), 100 umol/l deferoxamine mesylate, 20 umol/l leupeptide, etc. (p. 1254 col. 1; claims 84, 128, 129, 132). Ritov et al. do not specifically teach the role or function of deferoxamine in the composition. However, the properties of inhibiting microbial growth (claim 84) are properties that are inherent to deferoxamine.

Claims 84, 128, 129, 132 are rejected under 35 U.S.C. 102(b) as being anticipated by Meijs et al. (1996 Nuclear Medicine & Biology 23: 439-448). Claim 84, line 6, recites the weight ratio of albumin to pharmaceutical agent is about 18:1 or less. Therefore, the instant claim can encompass a weight ratio of 0. Meijs et al. teach a composition comprising BSA and desferal (Df) (p. 440 col. 1; claims 84, 128, 129, 132). It is known in the art that desferal is the brand name for deferoxamine. Meijs et al. do not specifically teach the role or function of deferoxamine in the composition. However, the properties of inhibiting microbial growth (claim 84) are properties that are inherent to deferoxamine.

Claims 84, 128-129, 132-133 are rejected under 35 U.S.C. 102(b) as being anticipated by Klebanoff et al. (1989 Journal of Biol Chem 264(33): 19765-19771). Claim 84, line 6, recites the weight ratio of albumin to pharmaceutical agent is about 18:1 or less. Therefore, the instant claim can encompass a weight ratio of 0. Klebanoff et al. teach a mixture comprising 8×10^{-6} M sodium iodide (4000 pmol), 0.2 mg/ mL human albumin, and deferoxamine (p. 19768). Klebanoff et al. do not specifically teach the role or function of deferoxamine in the composition. However, the properties of inhibiting microbial growth (claim 84) are properties that are inherent to deferoxamine.

Claims 84, 128, 129, 132, 182-183 are rejected under 35 U.S.C. 102(b) as being anticipated by Gutteridge et al. (1981 Journal of Inorganic Biochemistry 15: 349-357). Claim 84, line 6, recites the weight ratio of albumin to pharmaceutical agent is about 18:1 or less. Therefore, the instant claim can encompass a weight ratio of 0. Gutteridge et al. teach a

composition comprising bleomycin, ferrous ions, and desferrioxamine (p. 353; claims 84, 128, 129, 132, 182-183). It is known in the art that desferrioxamine is another name for deferoxamine. Gutteridge et al. do not specifically teach the role or function of deferoxamine in the composition. However, the properties of inhibiting microbial growth (claim 84) are properties that are inherent to deferoxamine.

Claims 84, 128, 129, 132, 182-183 are rejected under 35 U.S.C. 102(b) as being anticipated by Gutteridge (1984 Biochemical Pharmacology 33(19): 3059-3062). Claim 84, line 6, recites the weight ratio of albumin to pharmaceutical agent is about 18:1 or less. Therefore, the instant claim can encompass a weight ratio of 0. Gutteridge teaches a composition comprising streptonigrin, deoxyribose, and desferrioxamine (p. 3061 Table 2; claims 84, 128, 129, 132, 182-183). Gutteridge et al. do not specifically teach the role or function of deferoxamine in the composition. However, the properties of inhibiting microbial growth (claim 84) are properties that are inherent to deferoxamine.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 103, 104 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang et al. (1993 Biochem. Pharm. 46(2): 336-339) in view of current pharmaceutical practice. The

teachings of Yang et al. are outlined above. Yang et al. further teach that the composition comprising human serum albumin, dihydroartemisinin, and deferoxamine comprises human serum and Tris buffer in a 1:4 v/v (p. 336). Therefore, the composition of Yang et al. meets the limitation of 25% by weight of albumin (claim 103). Yang et al. do not teach said composition is dehydrated.

It is well known in the pharmaceutical arts that compositions can be readily dehydrated and/or lyophilized to create a stable product for storage and optionally reconstituted in solution for future use.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to lyophilize the composition of Yang et al. because one of ordinary skill would recognize that the components of the composition would remain the same lyophilizing said composition would create a stable product for storage (claims 103-104).

Claims 105, 106, 209 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ritov et al. (2001 Diabetes 50: 1253-1262) in view of current pharmaceutical practice. The teachings of Ritov et al. are outlined above. As noted above, Ritov et al. teach a composition comprising 100 mmol/l mannitol, 5.0 mg/ml bovine serum albumin (BSA), 100 umol/l deferoxamine mesylate, 20 umol/l leupeptide, etc. The weight/volume percent can often be used the percentage concentration. The molar mass of deferoxamine mesylate is 656.79 g/mol (art of reference: drugs.com, previously cited). Ritov et al. teach a 6.6×10^{-5} g/mL concentration of deferoxamine mesylate, that comprises 0.0066% by weight of deferoxamine mesylate in a 1 mL volume of the composition. Ritov et al. do not teach said composition is dehydrated.

It is well known in the pharmaceutical arts that compositions can be readily dehydrated and/or lyophilized to create a stable product for storage and optionally reconstituted in solution for future use.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to lyophilize the composition of Ritov et al. because one of ordinary skill would recognize that the components of the composition would remain the same lyophilizing said composition would create a stable product for storage (claims 105-106, 209).

Claims 107, 131, 152 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gutteridge et al. (1981 Journal of Inorganic Biochemistry 15: 349-357) in view of current pharmaceutical practice. The teachings of Gutteridge et al. are outlined above.

It is well known in the art that compositions can readily be formulated into different physical forms depending on the route of administration, i.e. capsules, tablets, solutions, oil-in-water emulsions, nanoparticles, etc.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to manufacture the composition of Gutteridge, which comprises bleomycin, ferrous ions, and desferrioxamine, into different formulations, i.e. emulsions, nanoparticles, because one of ordinary skill would recognize that the components of the composition would be the same and still exhibit the same properties except that it is in a different form (claims 107, 131, 152).

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marsha M. Tsay whose telephone number is (571)272-2938. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Maryam Monshipouri/
Primary Examiner, Art Unit 1656

March 13, 2008